● **TWO PATTERNS OF LONGITUDINAL MUSCLE ACTIVITY IN THE OPOSSUM LOWER ESOPHAGEAL SPHINCTER.** S.S. Harrington, W.J. Dodds, R.K. Mittal. Dept. of Medicine, University of Virginia Health Sciences Center, Charlottesville, Va.

The role of longitudinal muscle in lower esophageal sphincter (LES) function has not been thoroughly examined. We measured simultaneous longitudinal and circular muscle activity of the LES in 8 opossums. A miniature strain gauge transducer sutured onto the LES measured longitudinal muscle activity. Circular muscle activity was measured by intraluminal high-fidelity manometry which was done with a perfused catheter that incorporated a sleeve device to measure LES pressure. LES longitudinal and circular muscle activity were measured concurrently during nitroprusside infusion, and during vagal nerve stimulation before and after atropine. Longitudinal muscle contraction was measured in grams and LES pressure in mmHg. During nitroprusside infusion (1 µg/mint) there were significant decreases in LES longitudinal muscle activity, -1.8 ± 0.3 gms, and LES pressure -38.9 ± 2.2 mmHg. LES longitudinal muscle tone and LES pressure returned to basal levels following nitroprusside infusion. These observations suggest a tonic activity in LES circular as well as longitudinal muscle. 50 µg/kg atropine IV did not affect LES longitudinal muscle tone and LES pressure. Electrical stimulation (10 Hz, 5 mA, 0.5 msec pulse width) of the peripheral end of the right vagus nerve using 1 and 5 sec trains contracted LES longitudinal muscle and relaxed LES pressure. The duration of LES relaxation and longitudinal muscle contraction was related to the stimulus train length. Atropine decreased LES longitudinal muscle contraction and LES relaxation during vagal stimulation as shown below:

| | LES Longitudinal Muscle Contraction | | % LES pressure relaxation | |
|---|---|---|---|---|
| | 1 sec | 5 sec | 1 sec | 5 sec |
| pre-atropine | 3.6±0.1 | 5.6±0.2 | 79.7±3.7 | 77.3±4.4 |
| post-atropine | 0.6±0.3* | 2.5±0.4* | 57.7±4.7* | 76.2±2.9 |

Our results suggest two patterns of longitudinal muscle activity in the opossum LES: 1) a tonic longitudinal muscle contraction which is sensitive to nitroprusside, but resistant to atropine, 2) a vagally mediated LES longitudinal muscle contraction which is sensitive to atropine.

● **MECHANISM OF FELINE LOWER ESOPHAGEAL SPHINCTER OPENING DURING ESOPHAGEAL BOLUS TRANSPORT.** S.S. Harrington, W.J. Dodds, E.T. Stewart, J.G. Brasseur. Department of Radiology, Medical College of Wisconsin, Milwaukee, WI.

Although the manometric characteristics of lower esophageal sphincter (LES) relaxation have been well studied, the physical mechanisms of LES opening during esophageal emptying remain unknown. During laparotomy in 6 cats, we implanted tantalum markers onto the diaphragmatic hiatus and the margins of the LES segment. Two weeks later, secondary peristaltic sequences induced by proximal esophageal injection of a 4-ml barium bolus were recorded concurrently by manometry and videofluoroscopy, synchronized by a dual timer. Manometry was done using a high-fidelity recording system that incorporated a Dent sleeve device for recording LES pressure. LES pressure was also studied during spontaneous dry swallows, esophageal balloon distension, and external abdominal compression that increased intragastric pressure from basal levels to 20 mm Hg. Analysis showed that during peristalsis the LES slides through the diaphragmatic hiatus with a physiological herniation into the chest. Markers at the proximal marginal of the LES moved 12.2 ± 0.7 mm orad, 4.98 ± 0.6 mm above the hiatal markers. The LES relaxed during its deglutitive orad movement. Prior to sphincter opening, the head of the barium bolus transiently arrested for 0.70 ± 0.07 sec at the proximal margin of the relaxed, but closed LES. During esophageal peristalsis, pressure in the barium bolus gradually rose to approximate intragastric pressure before LES opening occurred. The interval between LES relaxation and LES opening, 3.0 ± 0.4 sec, increased significantly to 6.1 ± 0.5 sec during abdominal compression which increased intragastric pressure to 20 mm Hg. After esophageal emptying by peristalsis, LES pressure returned to its basal level and the LES markers gradually returned to their resting position. The LES moved proximally during esophageal balloon distension and dry swallows, but there was no physical LES opening. We conclude: 1) During esophageal peristalsis, the LES slides orad into the chest, becoming effaced over the bolus head prior to physical sphincter opening. 2) The LES is opened passively by an oncoming bolus. 3) A requisite for LES opening is that intrabolus pressure must equal or exceed the abdominal-thoracic pressure gradient which corresponds to intragastric pressure.

From the Midwest Dysphagia Institute (MDI)

Milwaukee, WI

● **ROLE OF THE PYLORUS IN THE PREVENTION OF DUODENO-GASTRIC REFLUX: EFFECTS OF THE SOMATOSTATIN ANALOG.** W. Hasler, H. Soudah, D. May, C. Owyang. Dept. of Int. Medicine, Univ. of Michigan, Ann Arbor, MI

The role of the pylorus as a barrier to duodenogastric (DG) reflux is controversial. Duodenal acid and lipids stimulate pyloric contractions. We investigated the ability of acid and lipid evoked pyloric motility to prevent DG reflux in healthy volunteers using a perfused manometrics catheter spanning the pylorus. Pyloric motility indices (MI) were calculated by measuring areas under the pressure curves. DG reflux was tested by a dual marker technique with duodenal phenol red perfusion (100mg/l at 2ml/min) and gastric polyethylene glycol (PEG) perfusion. Gastric aspirates were alkalinized and phenol red was spectrophotometrically measured (560nm) and corrected for PEG recovery. Gastric aspiration for total bile acids provided a 2nd measure of DG reflux. Duodenal perfusion of 0.1N HCl (2ml/min x 45min) increased pyloric MI 102±16% but did not affect duodenal motility. HCl perfusion decreased phenol red reflux 82±4% and reflux of bile acids into the stomach by 72±10%, showing that pyloric contractions alone can reduce DG reflux. Duodenal perfusion of 9% Microlipid (1.6kcal/min x 1hr) increased pyloric MI 219±25% and evoked a duodenal fed motor pattern. However lipid perfusion increased phenol red reflux 225±52% and gastric bile acids 866±180%, suggesting that lipid-stimulated pancreatico-biliary secretions overwhelmed the barrier capabilities of the pylorus. Somatostatin has profound motor effects on the upper gut. We next studied if the somatostatin analog octreotide affects DG reflux under basal and nutrient stimulated conditions. Octreotide (50µg sq) increased pyloric MI 54±10% and induced a coordinated duodenal pattern of alternating phase I and III activity with a period of 38±6 minutes which propagated aborally at 7.1±0.6cm/min. Octreotide decreased phenol red reflux 92±2% and gastric bile acids 65±15%. When duodenal lipids were perfused 45 minutes after octreotide injection, phenol red reflux and gastric bile acids were 94±2% and 96±5% lower than with lipid perfusion alone, confirming the analog can prevent DG reflux induced by duodenal nutrients. Conclusions: The pylorus has a role in preventing DG reflux but alone is inadequate in the postprandial state when there is increased pancreatico-biliary secretion. The somatostatin analog markedly decreases DG reflux under basal and nutrient stimulated conditions. The mechanism by which octreotide decreases DG reflux is multifactorial with inhibition of bile secretion as well as stimulation of pyloric motility and induction of aborally propagative duodenal motility.

**SOMATOSTATIN ANALOG INHIBITS AFFERENT RESPONSE TO RECTAL DISTENTION: INHIBITION OF N-TYPE CALCIUM CURRENT BY PERTUSSIS TOXIN SENSITIVE PATHWAY IN DORSAL ROOT GANGLIA.** W. Hasler, H. Soudah, J. Wiley, C. Owyang. Dept. of Int. Med. Univ. of Michigan, Ann Arbor, MI

Rectal distention leads to pressure, urgency and then pain. We investigated if the somatostatin analog octreotide modifies rectal sensory responses in healthy volunteers using anorectal manometrics. Double-blind injection of octreotide (100µg sq) vs. placebo was performed 45 mins prior to rectal balloon placement. Standardized questions were asked at progressive graded levels of inflation. With placebo injection, threshold sensation, moderate pressure, moderate urgency, and maximal tolerated volume were noted at 22±6, 80±10, 149±13,and 198±19ml inflation. With octreotide injection, threshold sensation, moderate pressure, moderate urgency, and maximal tolerated volume were detected at greater volumes than with placebo (58±6, 178±17, 300±23, and 370±23ml, $p<0.01$). As octreotide does not cross the blood-brain barrier, this inhibition in rectal sensation occurs peripherally. We showed octreotide increases rectal motility using solid state transducers confirming the decreased sensitivity to distention is not due to decreased rectal tone. To assess whether local rectal reflex arcs are involved, anal pressures were tested. Basal anal tone (76±2mmHg) and maximal squeeze pressures (177±8mmHg) were identical with placebo and octreotide. Rectal distention inhibited anal tone 36±5% at 10ml and 75±2% at 80ml inflation with placebo. This rectoanal inhibitory reflex was unchanged by octreotide showing that local rectal stretch receptors and reflex arcs are unaffected by the peptide. Thus octreotide acts on extrinsic innervation to the colon possibly at the spinal cord level. To evaluate if somatostatin affects afferent transmission in dorsal root ganglia (DRG), correlative studies of voltage-activated calcium currents were performed on enzymatically dispersed rat primary sensory DRG neurons using the whole cell patch clamp technique in media which block sodium and potassium currents. Somatostatin-14 (S14) (0.1nM-1µM) reduced N-type calcium currents 10±2 to 42±8%. Pertussis toxin pretreatment (100ng/ml x 12hrs) of cultured DRG neurons blocked the inhibitory effect of S14 on the N current component. Conclusions: Octreotide reduces sensation of rectal distention via a peripheral afferent pathway not involving rectal reflex arcs. In vitro experiments suggest that somatostatin may act by inhibiting N-type calcium currents in DRG neurons via pertussis toxin sensitive pathways. The inhibitory effect on peripheral rectal afferents may explain reported beneficial effects of the somatostatin analog on irritable bowel patients with rectal urgency.